Benz[a]anthracene (CASRN 56-55-3)

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Benz[a]anthracene; CASRN 56-55-3

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Benz[a]anthracene

File First On-Line 12/01/1990

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	no data	
Inhalation RfC Assessment (I.B.)	no data	09/01/1994
Carcinogenicity Assessment (II.)	on-line	03/01/1994

_I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

_I.A. Reference Dose for Chronic Oral Exposure (RfD)

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Not available at this time.

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_I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name -- Benz[a]anthracene
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Not available at this time.

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_II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name -- Benz[a]anthracene
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Last Revised -- 03/01/1994

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

_II.A. Evidence for Human Carcinogenicity

__II.A.1. Weight-of-Evidence Characterization

Classification -- B2; probable human carcinogen

Basis -- Based on no human data and sufficient data from animal bioassays. Benz[a] anthracene produced tumors in mice exposed by gavage; intraperitoneal, subcutaneous or intramuscular injection; and topical application. Benz[a]anthracene produced mutations in bacteria and in mammalian cells, and transformed mammalian cells in culture.

__II.A.2. Human Carcinogenicity Data

None. Although there are no human data that specifically link exposure to benz[a] anthracene to human cancers, benz[a]anthracene is a component of mixtures that have been associated with human cancer. These include coal tar, soots, coke oven emissions and cigarette smoke (U.S. EPA, 1984, 1990; IARC, 1984; Lee et al., 1976; Brockhaus and Tomingas, 1976).

__II.A.3. Animal Carcinogenicity Data

Sufficient. Benz[a]anthracene administration caused an increase in the incidence of tumors by gavage (Klein, 1963); dermal application (IARC, 1973); and both subcutaneous injection (Steiner and Faulk, 1951; Steiner and Edgecomb, 1952) and

Quantitative Estimate of Carcinogenic Risk from Oral Exposure

- Summary of Risk Estimates
- Dose-Response Data
- Additional Comments
- Discussion of Confidence

Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

- Summary of Risk Estimates
- Dose-Response Data
- Additional Comments
- Discussion of Confidence

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intraperitoneal injection (Wislocki et al., 1986) assays. A group of male B6AF1/J mice was exposed to gavage solutions containing 3% benz[a]anthracene in Methocel-Aerosol O.T. (dioctyl ester of sodium sulfo- succinic acid), 3 doses/week for 5 weeks (total dose of approximately 225 mg/mouse, 500 mg/kg/day) or the vehicle (Klein, 1963). Mice were evaluated for tumors on days 437-444 and 547 after treatment was initiated. A statistical analysis was not reported. Increased incidences of pulmonary adenoma and hepatoma in treated vs. control mice were reported by the authors at both observation times. The incidence of pulmonary adenoma at 437-444 days was 37/39 (95%) in treated animals vs. 10/38 (26%) in controls; whereas at 547 days, 19/20 (95%) treated animals and 7/20 (35%) controls had pulmonary adenomas. The incidence of hepatomas at 437 to 440 days was 18/39 (46%) in treated animals compared with 0/38 among the vehicle controls. After 547 days, the hepatoma incidences increased to 20/20 for the treated animals versus 2/20 (10%) for vehicle controls.

Mice (strain and sex not specified) were exposed to a single gavage dose of 0.5 mg benz[a]anthracene in mineral oil (approximately 17 mg/kg). No tumors were reported in 13 mice examined 16 months after exposure. In another part of the study, multiple gavage treatments, 8 or 16 treatments at 3-7 day intervals over a 16-month period, resulted in forestomach papillomas in 2/27 treated mice compared with 0/16 in vehicle controls (Bock and King, 1959).

Groups of male and female CD-1 mice (n=90-100) received intraperitoneal injections of benz[a]anthracene in DMSO on days 1, 8, and 15 of age (total dose = 638 ug/mouse) (Wislocki et al., 1986). Tumors were evaluated in animals that died spontaneously after weaning and in all remaining animals at 1 year after exposure. In treated male mice, a statistically significant increase in the incidence of liver adenomas or carcinomas (31/39 treated vs. 2/28 controls) occurred; 25/39 had carcinomas. Female mice did not develop liver tumors. The incidence of pulmonary adenomas or carcinomas in benz[a]anthracene-treated males (6/39, with a majority of adenomas) was increased but not statistically significantly relative to the vehicle controls (1/28). In the female mice, however, the incidence of pulmonary adenomas was significantly elevated in the treated group (6/32) when compared with vehicle controls (0/31).

Benz[a]anthracene yielded positive results in tests for complete carcinogenicity and initiating activity in skin painting assays in C3H/He, CAF1 and ICR/Ha mouse strains. These studies are reviewed in IARC (1973).

Subcutaneous injection of benz[a]anthracene in tricaprylin into C57Bl mice (40-50/group) produced injection site sarcomas 9 months after treatment (Steiner and Falk, 1951; Steiner and Edgecomb, 1952). The sarcoma incidences were: uninjected controls, 0/76; tricaprylin controls, 3/28 (11%); 0.05 mg, 5/43 (12%); 0.2 mg, 11/43 (26%); 1.0 mg, 15/31 (48%); 5.0 mg, 49/145 (34%); and 10 mg, 5/16 (31%). The results of similar experiments in this series were combined (Steiner and Edgecomb, 1952). A statistical analysis of the results was not reported. Survival was roughly equivalent in all groups (70%).

Klein (1952) showed that an intramuscular injection of benz[a]anthracene in combination with 1 or 3% croton oil produced injection site fibrosarcomas and hemangioendotheliomas in Strain A-derived albino mice; 3/24 mice injected with benz[a]anthracene and 1% croton oil and 1/26 mice injected with benz[a]anthracene and 3% croton oil developed tumors. None of the 30 mice injected with benz[a] anthracene and 0.1% croton oil and none of the 30 mice injected with benz[a] anthracene and 5% croton oil developed tumors. In the control groups none of the 35 mice injected only with 1% croton oil and none of the 32 mice injected only with benz [a]anthracene developed tumors. The survival rate for all groups was roughly equivalent (74%).

__II.A.4. Supporting Data for Carcinogenicity

The results of tests for DNA damage in Escherichia coli have not been positive at concentrations of benz[a]anthracene up to 250 ug/mL and 1000 ug/well (Rosenkrantz and Poirier, 1979; DeFlora et al., 1984). Positive results were obtained in tests for reverse mutation in five different strains of Salmonella typhimurium and for forward mutation in one strain (McCann et al., 1975; Coombs et al., 1976; Simmon, 1979; Salamone et al., 1979; Bartsch et al., 1980; DeFlora et al., 1984; Norpoth et al., 1984; Utesch et al., 1987; Bos et al., 1988; Kaden et al. 1979).

Benz[a]anthracene produced positive results in an assay for mutations in Drosophila melongaster (Fahmy and Fahmy, 1973).

Tests for DNA damage, mutation, chromosomal effects and cell transformation in a variety of eukaryotic cell preparations have yielded mostly positive results. Benz[a] anthracene tested positive for DNA damage in primary rat hepatocytes and HeLa cells (Probst et al., 1981; Martin et al., 1978). It also tested positive for forward mutation in Chinese hamster cells, V79 cells, mouse lymphoma L5178Y cells and rat liver epithelial cells (Slaga et al., 1978; Krahn and Heidelberger, 1977; Amacher et al., 1980; Amacher and Turner, 1980; Tong et al., 1981). Benz[a]anthracene tested positive for chromosomal affects in Chinese hamster ovary cells (Pal, 1981). Tests for cell transformation (cell morphology) have yielded positive results in Syrian hamster embryo cells and mouse prostate C3HG23 cells (Pienta et al., 1977; DiPaolo et al., 1969, 1971; Marquardt and Heidelberger, 1972).

Current theories on mechanisms of metabolic activation of polycyclic aromatic hydrocarbons are consistent with a carcinogenic potential for benz[a]anthracene. Benz[a]anthracene has a "bay-region" structure (Jerina et al., 1978). It is metabolized by mixed function oxidases to reactive "bay- region" diol epoxides that are mutagenic in bacteria and tumorigenic in mouse skin painting assays (Booth and Sims, 1974; Wood et al., 1977a,b).

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_II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

Not available.

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_II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

Not available.

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_II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

__II.D.1. EPA Documentation

Source Document -- U.S. EPA, 1984

The 1990 Drinking Water Criteria Document for Polycyclic Aromatic Hydrocarbons has received Agency and external review.

__II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review -- 02/07/1990, 08/05/1993, 09/21/1993, 02/02/1994

Verification Date -- 02/07/1990

__II.D.3. EPA Contacts (Carcinogenicity Assessment)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

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_VI. Bibliography

Substance Name -- Benz[a]anthracene
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_VI.A. Oral RfD References

None

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_VI.B. Inhalation RfC References

None

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_VI.C. Carcinogenicity Assessment References

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_VII. Revision History

Substance Name -- Benz[a]anthracene
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Date	Section	Description
12/01/1990	II.	Carcinogen assessment on-line
12/01/1990	VI.	Bibliography on-line
01/01/1992	IV.	Regulatory Action section on-line
09/01/1993	II.	Carcinogenicity assessment noted as pending change
09/01/1993	II.D.2.	Work group review date added
11/01/1993	II.D.2.	Work group review date added
03/01/1994	II.	Pending change note removed; no change
03/01/1994	II.D.2.	Work group review date added
09/01/1994	I.B.	Inhalation RfC now under review
08/01/1995	I.B., II.D.2.	EPA's RfD/RfC and CRAVE workgroups were discontinued in May, 1995. Chemical substance reviews that were not completed by September 1995 were taken out of IRIS review. The IRIS Pilot Program replaced the workgroup functions beginning in September, 1995.
04/01/1997	III., IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.

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_VIII. Synonyms

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Benz(a)anthracene
benz(a)anthracene
Benzanthracene
Benzanthrene
BENZO(a)ANTHRACENE
BENZO(b)PHENANTHRENE
Benzoanthracene
HSDB 4003
NSC 30970
RCRA WASTE NUMBER U018
Tetraphene
1,2-BENZ(a)ANTHRACENE
1,2-Benzanthracene
1,2-BENZANTHRAZEN [German]
1,2-BENZANTHRENE
1,2-BENZOANTHRACENE
2,3-Benzophenanthrene

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